

Received: 16 July 2024, Accepted: 21 August 2024

FREQUENCY OF HEPATITIS C-VIRUS CO-INFECTION IN HIV-INFECTED PATIENTS IN TERTIARY CARE HOSPITALS IN LAHORE, PAKISTAN

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ABSTRACT

Background: The coinfection of Hepatitis C-Virus (HCV) in patients of Human Immunodeficiency Virus (HIV) infection occurs commonly owing to the same route of transmission. The prevalence of HCV/HIV coinfection in western population has an estimated number of around 5 to 10 million people. More deaths are being attributed to liver related causes than AIDS in HIV infected patients. There is not much of data available with respect to prevalence of HCV/HIV coinfection in Pakistan. Single major culprit responsible for coinfection of HIV/HCV has been identified as IV drug usage. However, Men having Sex with Men (MSM) have become another population at higher risk for HCV coinfection among HIV infected patients.

Objective: This study aims to find out the frequency of HCV co-infection in HIV-infected patients registered in Tertiary care hospitals of Lahore.

Methodology: The study was a cross-sectional analytical study which was conducted between January 1, 2023 and June 15, 2023. The patients selected for this study were the persons who reported to the 3 HIV clinics in tertiary care hospitals in Lahore

Results: The results have indicated that out of 372 HIV infected patients, 182 patients (48.9%) had HCV coinfection which is a very high percentage. Strong association has been found between HCV/HIV coinfections and IV drug usage which is consistent with earlier studies.

Conclusion: This study has indicated that there is a high frequency of HCV co-infection among HIV infected patients in Lahore. This study has also found significant variations in test results of patients reporting to different hospitals in Lahore.

Key words: hepatitis C virus, human immunodeficiency virus (HIV), mortality, anti-retro viral therapy, Sexually Transmitted diseases

INTRODUCTION:

Hepatitis infection of HCV, Hepatitis Virus-B infection (HBV) and human immunodeficiency virus infection (HIV) are included in 10 deadliest infectious diseases across the world¹. HIV infection, in particular, has been rising since the start of epidemic. According the Joint United Nations Programme on HIV/AIDS (UNAIDS), globally, the number of people living with HIV in 2021 was 38.4 million while there were around 1.5 million new infections of HIV in 2021². It is estimated that the number of people infected with HIV has risen to 84.2 million since this epidemic began.

The incidence and prevalence of HIV in Pakistan are relatively low compared to many other countries, but a steady increase has been observed in recent years. However, the actual number of cases may be higher due to underreporting and limited testing. In addition, association of stigmas and meting out discrimination against people who are living with an infection of HIV can contribute to a reluctance to seek testing and treatment, which further compounds the problem³.

In Pakistan, the number of people living with an infection of HIV was estimated at 210,000 in 2021 with a vast majority (over 80%) of them being males at 170,000². Pakistan has a concentrated epidemic of HIV infection, which means that the virus is mainly transmitted through populations who are at higher risk of infection, such as people who use drugs through intravenous routes, male & female sex workers, and MSM^{4,2}. However, there is evidence of an increasing number of cases in the general population. The annual number of new HIV infections in Pakistan has increased from 8,000 in 2010 to 22,000 in 2020, which represents an incidence rate of approximately 0.1%. The main modes of transmission of HIV in Pakistan are injecting drug use and sexual transmission⁵.

According to the National AIDS Control Programme (NACP) of Pakistan, as of March 2023, there were around 0.2 million cases of HIV infection in the country⁶. Of these cases, 57,505 knew about their HIV status till June, 2022 whereas 35,877 persons were on ARV therapy. The majority of the reported cases (approximately 60%) have been in the province of Sindh, which includes the city of Karachi, followed by Punjab province (approximately 30%)^{7,8,5}. The HIV prevalence among high-risk populations in Pakistan is particularly high. According to UNAIDS, the HIV prevalence among people who inject drugs in Pakistan was 27%, while the prevalence among sex worker females was 2.7% and among men who do sex with men was 5.7%^{9,2}.

Despite these high numbers, it is worth noting that HIV remains a serious public health concern in Pakistan, and it is likely underreported in the country due to social stigmas attached, and the true number of cases may be higher^{9,10}. In addition, access to testing and treatment for HIV is limited, particularly among key populations, which can contribute to ongoing transmission of the virus^{11,10}.

HCV is a bloodborne virus which transmits through coming into direct contact with an infected person's blood. HCV / HIV coinfection is fairly common (62%–80%) among HIV-infected injected drug users¹². The prevalence of patients having infection of human immunodeficiency virus (HIV) carrying the hepatitis C virus (HCV) contemporaneously ranges worldwide between 10% and 50%. This wide range reflects that in different countries HCV infection has different diffusion and HCV transmission-related environmental factors have a different impact¹³. Chronic HCV infection in

approximately 1/3rd of patients progresses to cirrhosis within a median time of <20 years. This progression rate is increased significantly by factors including alcoholism, HIV infection, older age, and male sex. In the developing countries, a higher prevalence of HCV/HIV coinfection (HCV coinfection among patients already infected with HIV) with geographically disproportionate variation (0% to 22%) in sub-Saharan Africa is seen¹⁴. World over, an estimated population of 71 million people have a chronic infection of HCV, and out of them, 5 million people have a coinfection of HCV / HIV^{15,16}.

Coinfection of HCV is reported commonly among HIV-infected patients and has an association with higher HCV RNA and expeditious progression of liver disease than in comparison with HCV infection cases alone¹⁶. Compared with either HCV or HIV infections alone, HCV/HIV coinfection is associated with various liver diseases, organ dysfunction (non-hepatic), or even death¹⁷. HCV/HIV coinfection also makes antiviral treatment complicated because of its side effects including hepatotoxicity, a resistance to antiviral drugs as well as suboptimal drug response^{19,20}.

This research study is aimed at investigating the frequency among patients infected with HIV. Despite the major advancements in healthcare, HCV coinfection remains a major policy concern for healthcare sector. Understanding of the frequency and associated factor is required for informed policymaking aimed at prevention, early diagnosis, and appropriate and timely treatment. The research focuses on two aspects, Determine frequency of HCV coinfection among HIV infected patients.

Objectives of the study

This study's aims to find out the prevalence of co-infection of HCV in patients having infection of HIV registered in Tertiary care hospitals of Lahore and the associated factors to determine the burden of this disease.

Methodology: The study was a cross-sectional analytical study which was conducted between January 1, 2023 and June 15, 2023. The patients selected for this study were the persons who reported to the 3 HIV clinics in tertiary care hospitals in Lahore. The Inclusion Criteria for participants selection (HIV positive patients, Patients having age ≥ 18 years themselves or <18 years through their parents/guardians, Regardless of Gender (i.e., including Male/Female/Transgender) and Patients presenting in HIV clinics and OPDs Of three tertiary care Hospitals Lahore but the Exclusion Criteria of participants Patients having hepatitis C before the diagnosis of HIV, Patients having TB or other infections other than HCV, Critical Health Condition and Patients presenting in HIV clinics and OPDs of Other Tertiary care Hospitals of Lahore. The size of sample calculated for this study was 372 taking anticipated population proportion of HCV co-infection through convenience sampling. All data thus collected was analyzed using SPSS version 27 and presented in the form of frequency, percentage and mean \pm SD.

RESULTS

372 patients have been recruited in this study with their consent. Of these, a vast majority 319 were males (85.8%) while only 38 were females (10.2%), and 15 were transgender (4.0%).

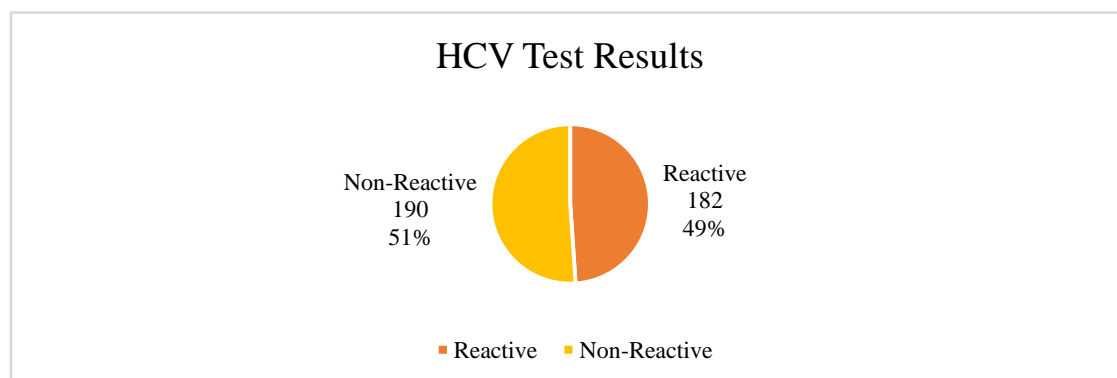
Out of 372 patients, 182 patients (48.9%) returned Positive test results for HCV. This is a very high percentage as compared to other regions, but other studies have suggested higher prevalence of

HCV infection in overall population in Pakistan (WHO, 2016) and the high HCV coinfection prevalence in HIV-infected patients in Pakistan (41%) has been reported in another study (Shahzad et al., 2021).

Table Error! No text of specified style in document.-1 HCV Tests Results showing patients infected with HIV as having HCV coinfection

HCV Test Result		
	Frequency	Percent
Positive	182	48.9
Negative	190	51.1
Total	372	100.0

Figure Error! No text of specified style in document.-1 HCV Test Results Chart showing frequency of 48.9% HCV coinfection in HIV infected patients



4.1.1 Age Distribution

The mean age for the participants turned out to be 33.6 years with Standard Deviation of ± 8.49 . The minimum age of participants was 16 while the maximum age was 65 years.

Table Error! No text of specified style in document.-2 Age Distribution Statistics showing minimum and maximum ages of participants

Age Distribution Statistics	
Age	Number of Patients
Mean \pm Std.deviation	33.6 \pm 8.495
Minimum	18
Maximum	65

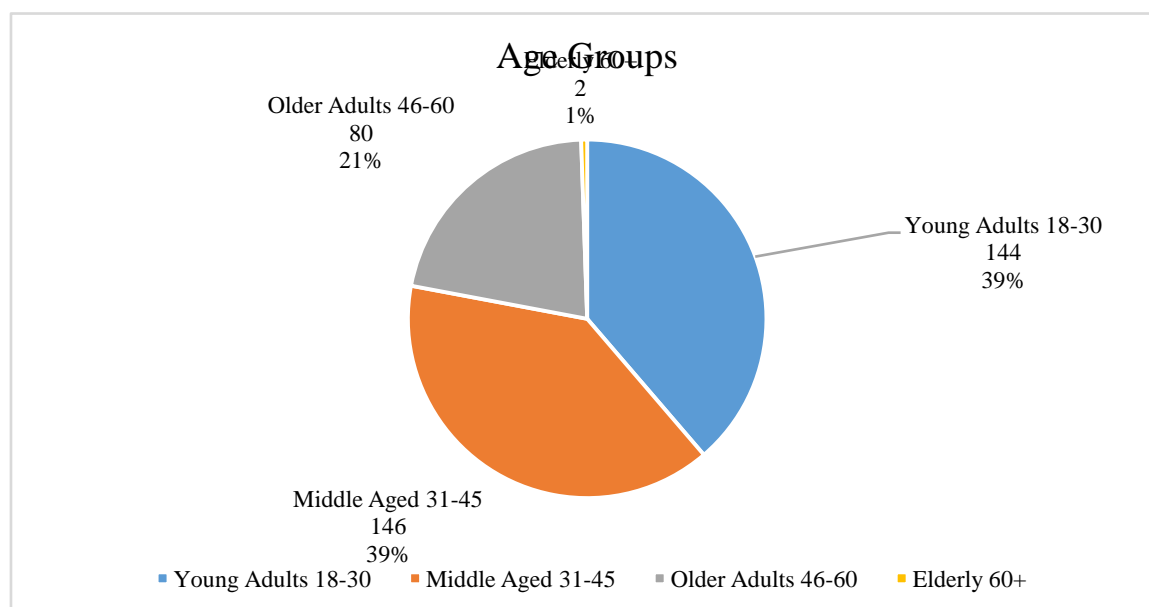
Figure **Error! No text of specified style in document.**-2 Histogram showing Distribution of data on the basis of age in years

The age group of Middle Aged 31 to 45 had maximum number of patients, i.e., 146 (39.2%), followed closely by Young adults aged 18 to 30 years old with 145 patients (38.7%). Older Adults were 146 patients (39.2%). While in Elderly patients 60+ category there were 2 patients (0.5%).

Table **Error! No text of specified style in document.**-3 Data of Age Groups showing that majority of population belonged to Young Adults and Middle-aged adults

Age Group		
	Frequency	Percent
Young Adults 18-30	144	38.70
Middle Aged 31-45	146	39.2
Older Adults 46-60	80	21.5
Elderly 60+	2	.5
Total	372	100.0

Figure Error! No text of specified style in document.-3 Pie chart showing Age Groups Distribution with most participants in two categories of Young Adults and Middle-aged Adults



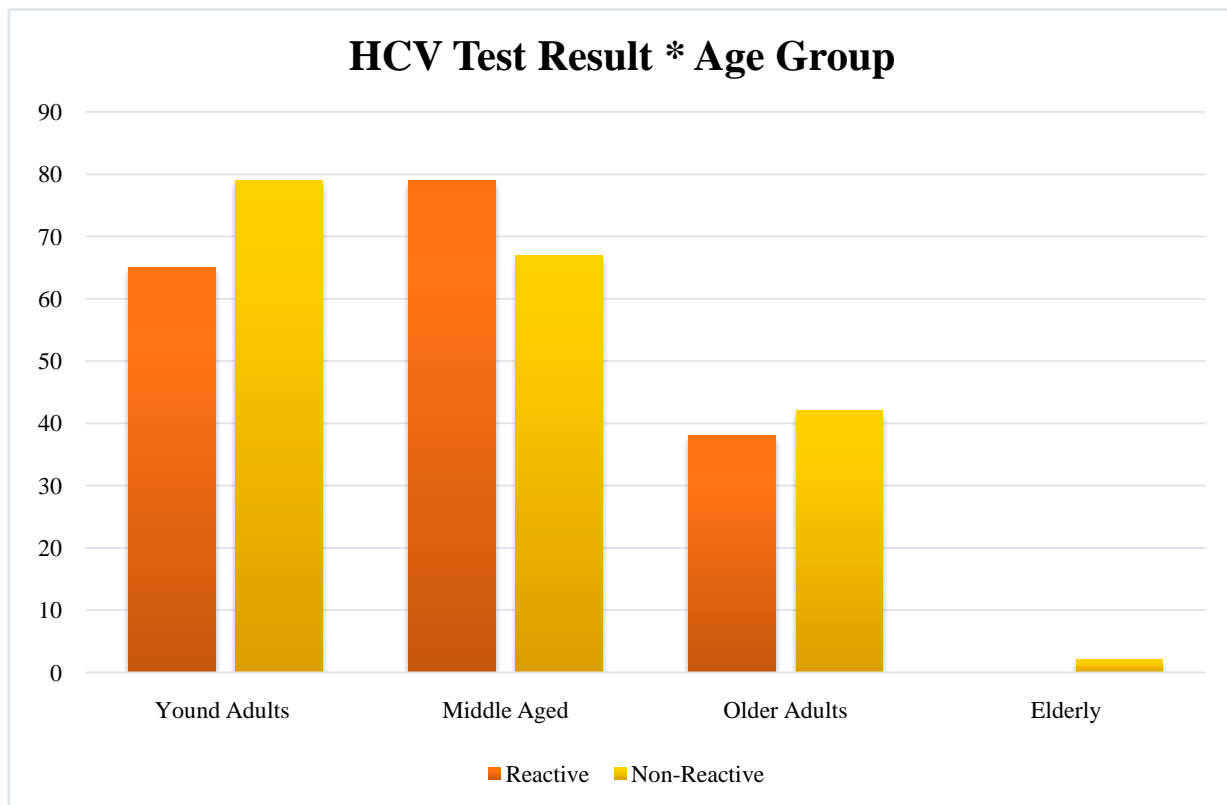
HCV Test Result in comparison of participants according to their Age Group

Table Error! No text of specified style in document.-4 HCV Results according to Age Groups showing that majority of middle-aged persons (54.1%) returned positive results for HCV coinfection which is more than the overall frequency of HCV coinfection

		Age Group				
		Young Adults 18-30 years	Middle Aged 31-45 years	Older Adults 46-60 years	Elderly 60+ years	Total
HCV Test Result	Positive	65 (45.13%)	79 (54.1%)	38 (47.5%)	0 (0%)	182 (48.9%)
	Negative	79 (54.87%)	67 (45.9%)	42 (52.5%)	2 (100%)	190 (51.1%)
Total		144 (38.7%)	146 (39.2%)	80 (21.5%)	2 (0.5%)	372

Results have indicated no association between HCV coinfection and gender (P value more than .05). Based on age groups, majority were Middle-aged persons of 31-45 years age of whom 79 patients (54%) returned Positive results for HCV whereas 67 patients (46%) returned Negative results. Next large group were Young adults aged 18-30 years of whom, 45.1% (65 patients) were Positive and 79 patients (54.9%) were Negative. Among Older adults (46-60 years of age) category, 47.5% (38 patients) were Positive and 42 patients (52.5%) were Negative. There were 2 patients in Elderly (Above 60 years) category and all of them returned Negative results for HCV.

Figure Error! No text of specified style in document.-4 HCV Results according to Age Groups showing that majority of middle-aged persons (54.1%) returned positive results for HCV coinfection which is more than the overall frequency of HCV coinfection



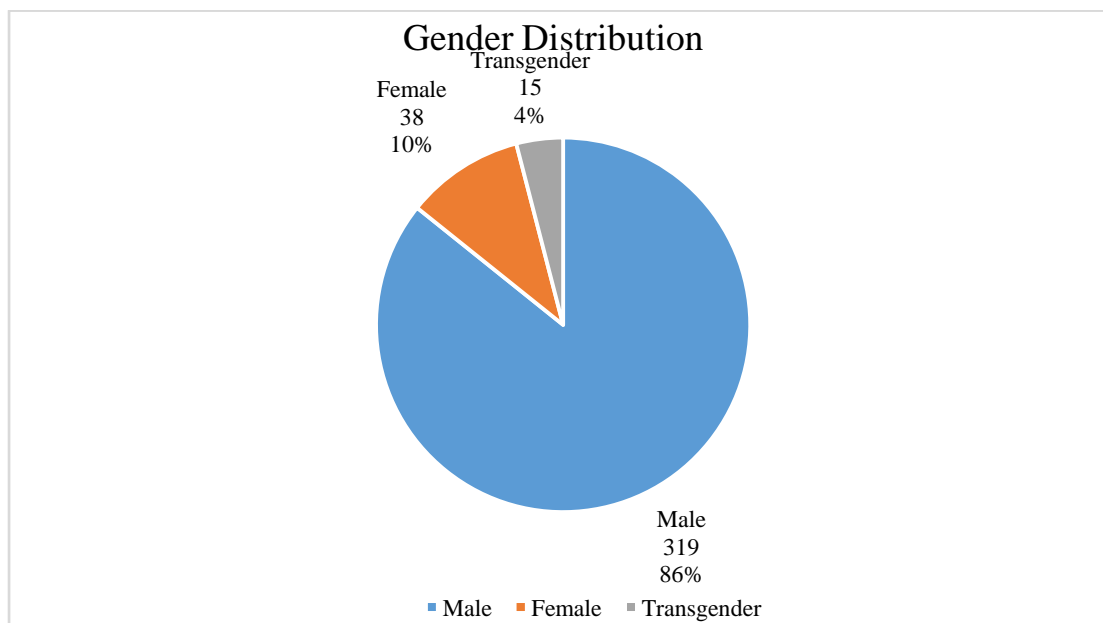
4.1.2 Gender Distribution

The 372 patients whose surveys were completed, 38 were females (10.2%), 319 were males (85.8%), and 15 were transgender (4.0%).

Table Error! No text of specified style in document.-5Data of gender distribution showing that a vast majority (85.8%) of population were males

Gender Distribution		
	Frequency	Percent
Male	319	85.8
Female	38	10.2
Transgender	15	4.0
Total	372	100.0

Figure Error! No text of specified style in document.-5 Pie chart of gender distribution showing that a vast majority (85.8%) of population were males



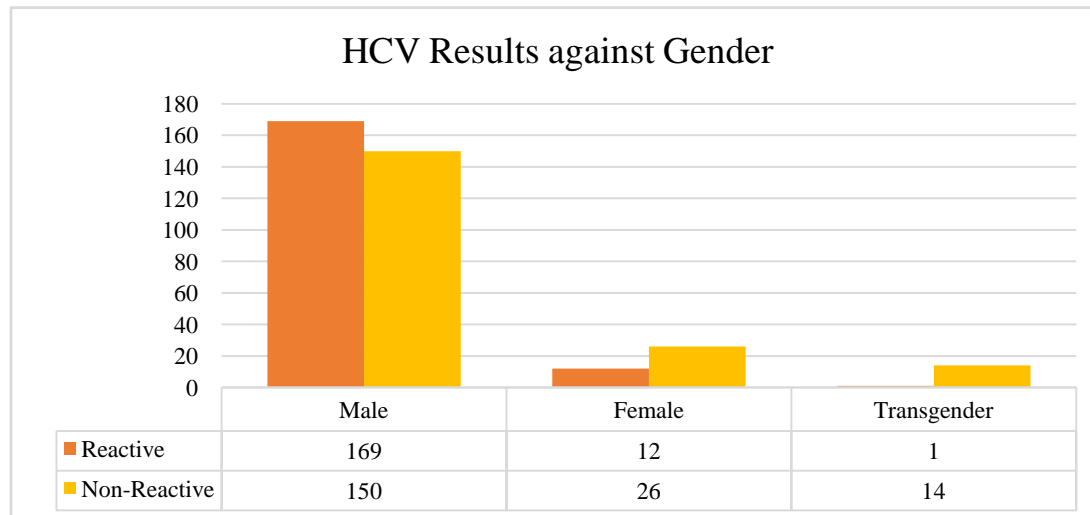
HCV Test Result based on Gender

Table Error! No text of specified style in document.-6HCV Results according to Gender distribution showing that majority of male patients (52.97%) returned positive results for HCV coinfection which is more than the overall frequency of HCV coinfection (48.93%)

		Gender			Total
		Male	Female	Transgender	
HCV Test Result	Positive	169 (52.97%)	12 (31.6%)	1 (6.67%)	182 (48.93%)
	Negative	150 (47.03%)	26 (68.4%)	14 (93.33%)	190 (51.07%)
Total		319 (85.75%)	38(10.25%)	15 (4.0%)	372

Results have indicated that in this study, more male patients developed association between HCV coinfection (P value less than .05) than other genders.

Figure Error! No text of specified style in document.-6HCV Results according to Gender distribution showing that majority of male patients (52.97%) returned positive results for HCV coinfection as compared to female and transgender patients



Among the genders, only 1 enrolled Transgender patient returned Positive results for HCV whereas 14 returned Negative results, while all of them had HIV-positive results. Among Females, 31.5% (12 patients) were Positive and 26 patients (68.5%) were Negative. Among Males, 53% (169 patients) were Positive and 150 patients (47%) were Negative.

Figure Error! No text of specified style in document.-7HCV Results in Females showing less frequency as compared to overall results

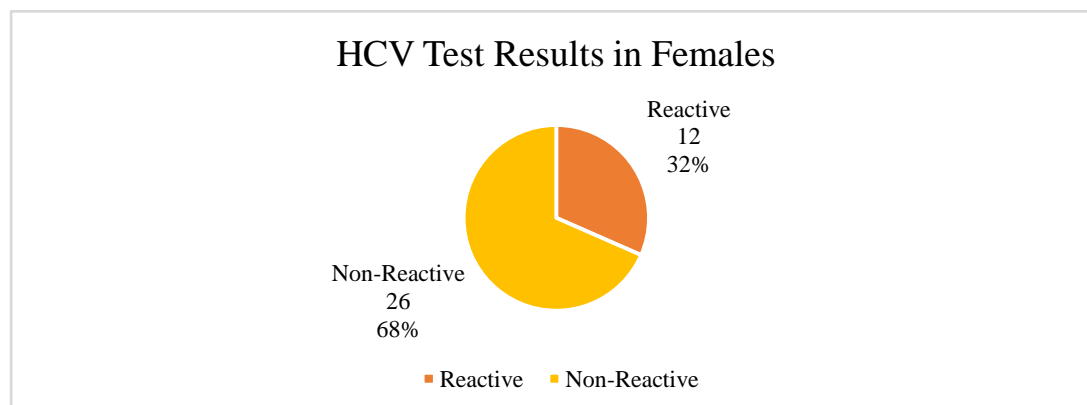


Figure Error! No text of specified style in document.-8HCV Results in Males showing more frequency as compared to overall results

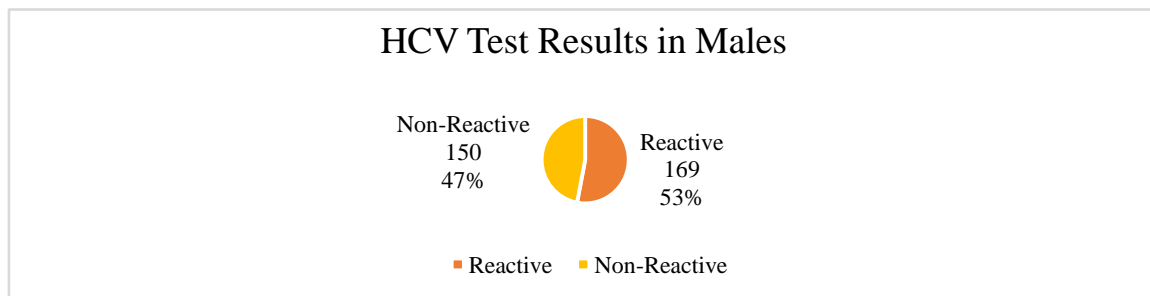
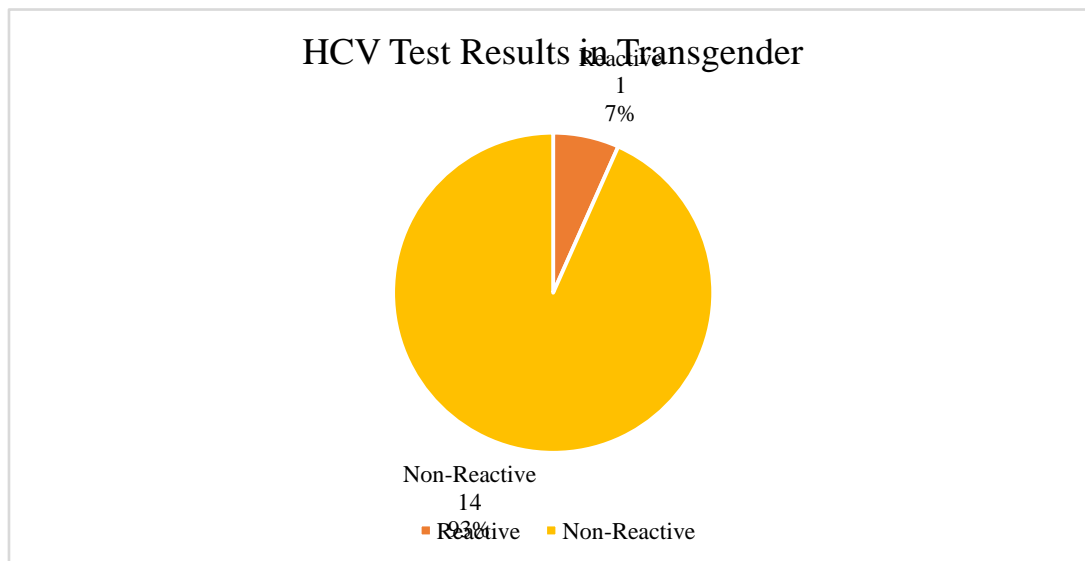


Figure Error! No text of specified style in document.-9HCV Results in Transgender showing less frequency as compared to overall results

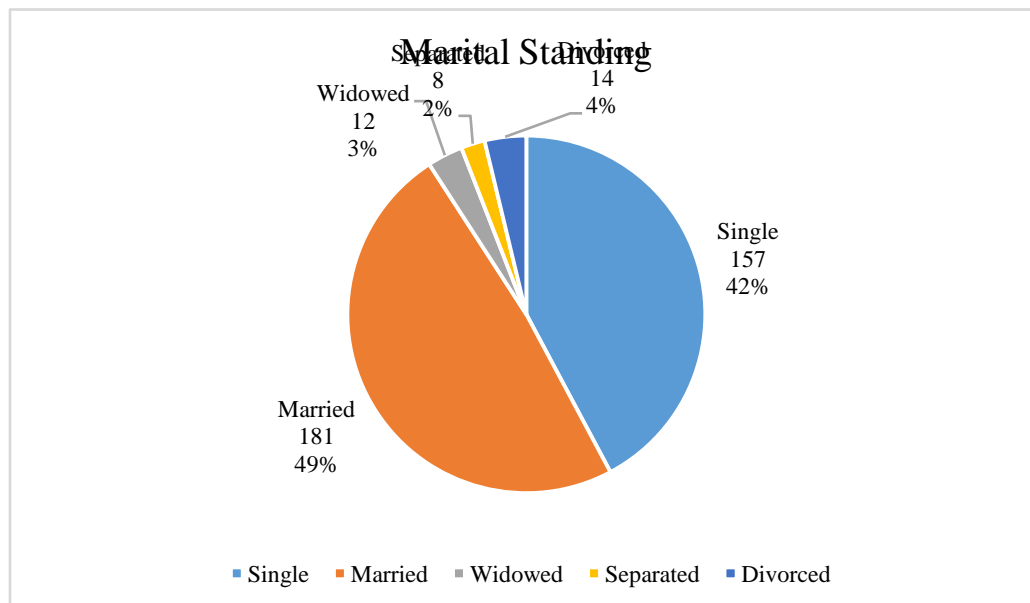


4.1.3 Marital Status

Table Error! No text of specified style in document.-7Marital Standing of participants showing most patients were from married category followed by Singles

Marital Standing		
	Frequency	Percent
Singles	157	42.2
Married	181	48.7
Widowed	12	3.2
Separated	8	2.2
Divorced	14	3.8
Total	372	100.0

Figure Error! No text of specified style in document.-10Pie chartMarital Status of participants showing most patients were from married category followed by Singles



Of the 372 registered patients, majority i.e., 181 patients (49%), were married. Singles were the second largest category with 157 patients (42%). 14 patients (3.8%) were divorced, 12 patients (3.2%) were widowed and 8 patients (2.2%) were separated in their marital lives.

HCV Test Result based on Marital Status

Based on Marital status, majority were married persons of whom 82 patients (45%) returned Positive results for HCV whereas 99 patients (55%) returned Negative results, while all of them had HIV-positive results. Among Singles category, nearly 50% (78 patients) were Positive and 79 patients (50%) were Negative. Among widowed category, again 50% (6 patients) were Positive and 6 patients (50%) were Negative. All 8 patients who had been separated returned Positive test results for HCV. Among divorced patients, 8 were Positive (57%) and 6 (43%) were Negative.

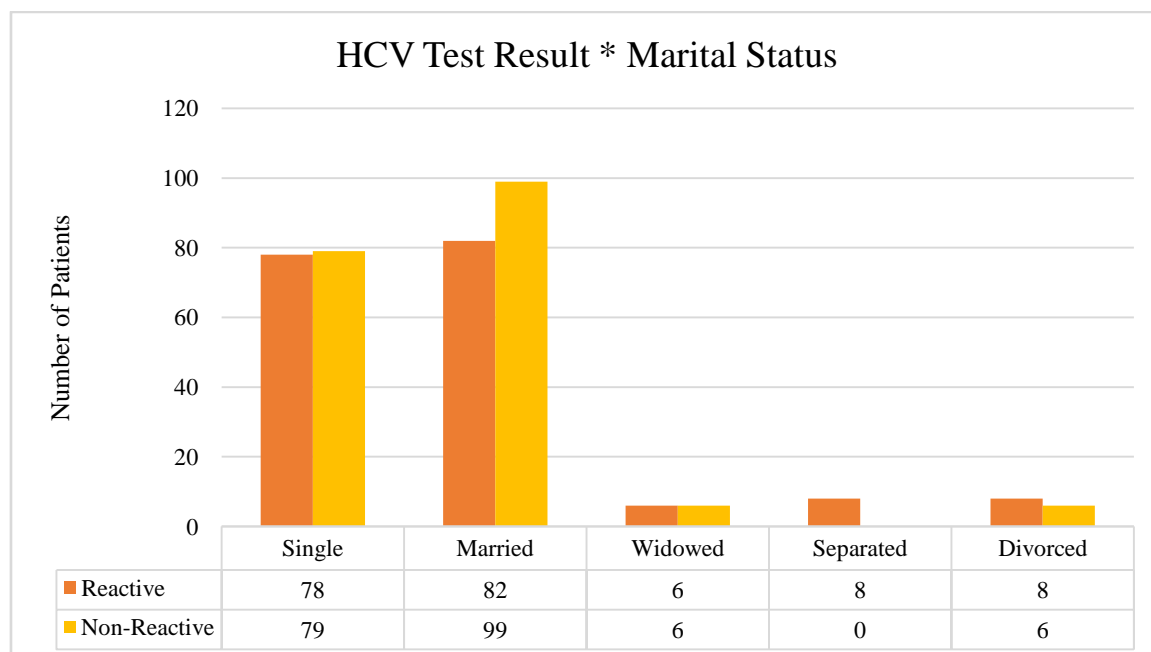
Table Error! No text of specified style in document.-8HCV Results against Marital Status indicating that the married individuals are less prone to HCV coinfection in HIV infected patients than patients with other marital status

		Marital Status					Total
		Single	Married	Widowed	Separated	Divorced	
HCV Test Result	Positive	78 (49.7%)	82 (45.3%)	6 (50%)	8 (100%)	8 (57.14%)	182 (48.9%)

	Negative	79 (50.3%)	99 (54.7%)	6 (50%)	0 (0%)	6 (42.86%)	190 (51.1%)
Total		157 (42.2%)	181 (48.7%)	12(3.22%)	8 (2.15%)	14 (3.76%)	372

Results have indicated association between HCV coinfection and marital status (P value less than .05). Separated and Divorced individuals are more prone to HCV coinfection than patients having other marital status in HIV infected population. The most patients were in married persons' category and they had the least frequency of positive HCV test results.

Table Error! No text of specified style in document.-9HCV Test Results against Marital Status indicating that the Separated and Divorced individuals are more prone to HCV coinfection



4.1.4 Education Level

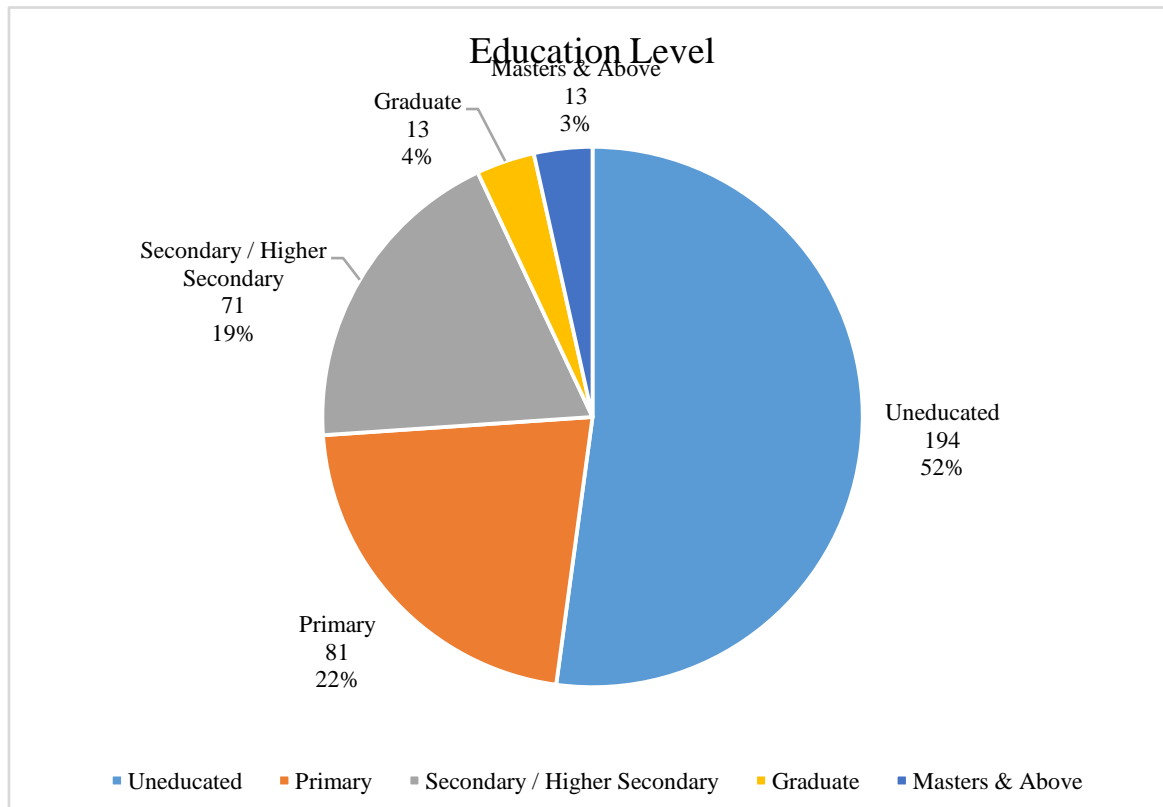
Of the 372 registered patients, majority i.e., 194 patients (52.2%), were uneducated. Patients with primary level education were the second largest category with 81 patients (21.8%) followed by patients with Secondary or Higher Secondary level education with 71 patients (19.1%). 13 patients (3.5%) each were registered who had Bachelors and Masters & above level of education.

Table Error! No text of specified style in document.-10Level of Education in Patients indicating that most of the HIV patients are from uneducated class

	Frequency	Percent
Uneducated	194	52.2
Primary	81	21.8
Secondary / Higher Secondary	71	19.1

Graduate	13	3.5
Masters & Above	13	3.5
Total	372	100.0

Figure Error! No text of specified style in document.-11 Level of Education in Patients indicating that most of the HIV patients are from uneducated class



HCV Test Result based on Education Level of Patients

Based on Education level, majority were uneducated persons of whom 107 patients (55.15%) returned Positive results for HCV whereas 87 patients (44.85%) returned Negative results. Next large group were Primary level literate people of whom, 49.38% (40 patients) were Positive and 41 patients (50.62%) were Negative. Among Secondary / Higher Secondary level literate category, 42.25% (30 patients) were Positive and 41 patients (57.75%) were Negative. There were 13 patients in Graduate category, of whom, 23.07% (3 patients) were Positive and 10 patients (76.93%) were Negative. There were 13 patients in Masters & above category, of whom, 15.38% (2 patients) were Positive and 11 patients (84.62%) were Negative.

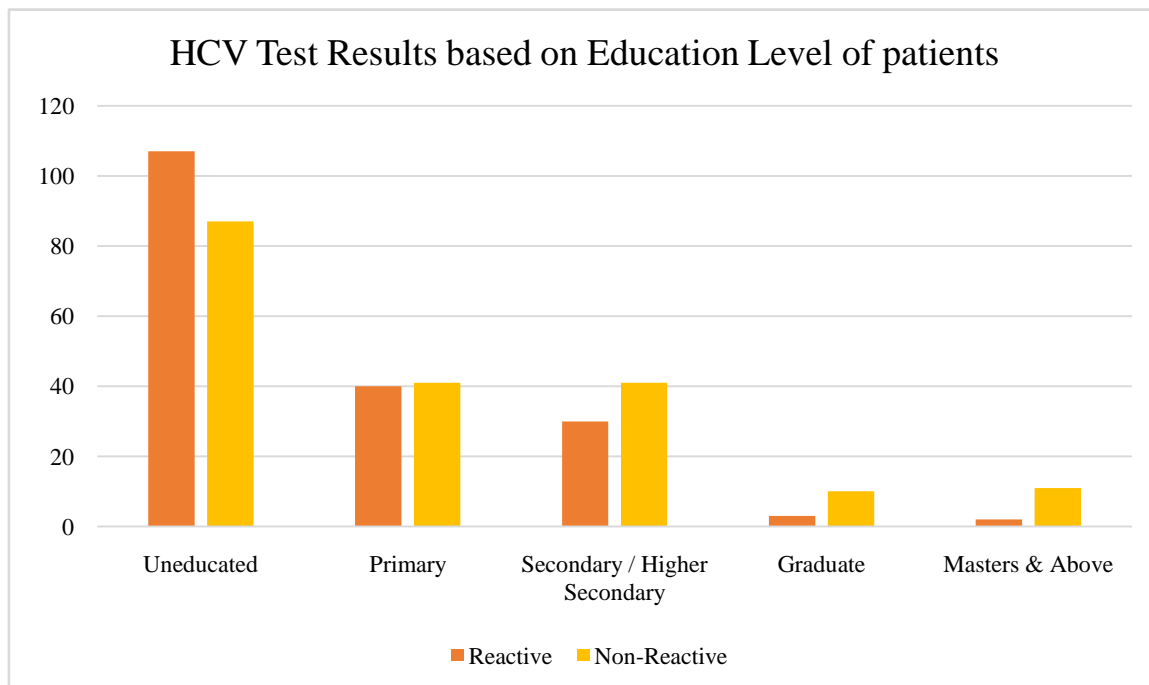
Table Error! No text of specified style in document.-11 HCV Test Result based on Education Level of patients indicating that

	Education Level	
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		Uneducated	Primary	Secondary / Higher Sec.	Graduate	Masters & Above	Total
HCV Test Result	Positive	107 (55.15%)	40 (49.38%)	30 (42.25%)	3 (23.08%)	2 (15.38%)	182 (48.92%)
	Negative	87 (44.84%)	41 (50.62%)	41 (57.74%)	10 (76.92%)	11 (84.61%)	190 (51.08%)
Total		194 (52.15%)	81 (21.77%)	71 (19.08%)	13 (3.49%)	13 (3.49%)	372

Results have indicated association between HCV coinfection and education level of patients (P value less than .05). Uneducated patients are more prone to HCV coinfection than patients having higher educational qualification in HIV infected population. The results indicated that patients having Masters & above qualifications had least frequency (15.38%) of HCV coinfections followed by graduate patients (23.08%) as compared to overall frequency of 48.9%.

Figure Error! No text of specified style in document.-12HCV Test Result based on Education Level in HIV infected patients indicating that uneducated patients are more prone to HCV coinfection than patients with higher education



Discussion

Among the 372 patients infected with HIV recruited in this study, 182 patients (48.9%) returned Positive results for HCV. This percentage is higher than those reported earlier but it may be due to the fact that the population recruited in this study came from Tertiary care hospitals where normally referred patients go. Earlier studies have indicated a very high prevalence of infection of HCV in overall population in Pakistan. Considering that Pakistan has among the highest prevalence rates of HCV infection in overall population in the world^{21, 22}, a frequency of 48.9% is understandable in a population at higher risk of HIV infected population.

A high rate of Injection Drug usage was identified among those who were co-infected. Similarly, higher rates of co-infection were seen in the category of Men who do Sex with other Men. These findings are consistent with earlier studies which have indicated that one of the major factors in HCV infection in Pakistan is the sharing of needles in people who have intravenous injected drugs. In this study, 81.3 % patients who were HCV Positive had a history of injected drug use. Furthermore, 82% HIV infected patients who had a history of injected drug use were also Positive for HCV infection. This rate is double the earlier rate²³ set for this study. This is also significant because the number of patients in this study with a positive history of injected drug use were almost half of total registered patients.

Other factors found significant in this study include Gender whereby it has been noted that male patients in this study developed HCV coinfection more frequently than other two genders. Furthermore, education level has been found to be associated with HCV coinfection. Frequency of positive HCV coinfection result was found to be highest in uneducated patients. Moreover, marital

status also indicated association with HCV results. Separated and divorced patients were found to be at more risk than other patients. HCV coinfection rates were lowest in married people.

LIMITATIONS OF STUDY

This study has examined the frequency and risk factors of coinfection of HCV in patients infected with HIV only. It does not cover the prevalence and risk factors of coinfection of HCV in overall population which also has been very high for Pakistan.

Another limitation of this study has been that it does not compare the frequency and risk factors of coinfection of HCV in patients infected with HIV with those patients who turned out to be HIV negative.

Beside this an important limitation is the sample size and location of this study in Lahore where most of the population has been from Lahore city. It therefore, does not cover the peripheral, rural areas and other regions.

Conclusion

The coinfection of Human Immunodeficiency Virus (HIV) and Hepatitis Virus-C (HCV) is frequent owing to the same route of transmission. This study has indicated that there is a high frequency of HCV co-infection among HIV infected patients in Lahore. This study has also found significant variations in test results of patients reporting to different hospitals in Lahore.

RECOMMENDATIONS

- Regular screening programs for hepatitis in general population
- Special screening for higher risk population including injected drug users
- Monitored treatment regimens for higher risk population including injected drug users and MSM

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